DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Our Reference No.: 99-0128

November 10, 1999

Mr. Martin Page
Centocor, Inc.
200 Great Valley Parkway
Malvern, PA 19355

Dear Mr. Page:

Your request to supplement your biologics license application for Infliximab to include a new indication for reduction in signs and symptoms of rheumatoid arthritis in patients who have had an inadequate response to methotrexate has been approved.

As of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred
(63 *FR* 66632).

We acknowledge your written commitments of July 9, 1999, September 8, 1999, and November 4, 1999, which include the following:

1. To develop an assay to measure rheumatoid factor reactivity to Infliximab (IFX-RF) and perform the analysis on serum samples from patients in the ATTRACT study. We note that development of this assay has commenced and that results will be submitted by June 2000.

2. To continue a three-year, long-term safety follow-up and provide the information to the Center on a periodic basis, at least annually. This commitment includes obtaining long-term safety information on malignancies, deaths, autoimmune disorders and delayed hypersensitivity for three years and serious infections for six months after patients have received their last infusion of Infliximab. If additional safety concerns are identified after this period, the Center may, in consultation with Centocor, require an extension and/or modification of the safety follow-up.

3. To conduct a juvenile rheumatoid arthritis clinical study.

4. To submit a proposal by June 2000 as to how Centocor will evaluate the response to immunizations in Infliximab-treated patients.

5. To demonstrate that the relative reactivity of the [redacted] as defined by reactivity with BSA-deficient media, is proportional to the [redacted] content in a non-secreting, transfected cell line cultured in the same medium.

6. To perform spiking studies to validate the ability of the Infliximab purification process to remove [redacted] and to continue testing individual lots of [redacted] until these validation studies are completed.

7. To develop an assay to measure serum antibodies to bovine IgG which will be used to assay serum samples from patients who participated in Centocor's C0168T24 trial. The assay will be developed by July 2000 and results from the T24 samples will be submitted by August 2000.

Please submit three copies of final printed labeling at the time of use and include part II of the label transmittal form (FDA form 2567) with completed implementation information. In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 or Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2567 or Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

This information will be included in your biologic license application file.

Sincerely yours,

Karen D. Weiss, M.D.
Director
Division of Clinical Trial
Design and Analysis
Office of Therapeutics
Research and Review
Center for Biologics
Evaluation and Research